Giant Dedifferentiated Liposarcoma of the Mediastinum

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AIM: Soft tissue sarcomas are rare, accounting for only 1% of adult malignancies, with liposarcoma being a common subtype. However, mediastinal liposarcomas are extremely uncommon, comprising less than 1% of cases. Dedifferentiated liposarcoma (DDLPS) is a particularly aggressive variant, characterized by a transition from well-differentiated to high-grade non-lipogenic sarcoma. Due to its rarity and often asymptomatic nature until significant progression, mediastinal DDLPS presents a unique diagnostic and therapeutic challenge.

CASE PRESENTATION: An 83-year-old woman with ischemic heart disease presented with progressive dyspnea over two months. Imaging revealed a giant, well-circumscribed mediastinal mass (21 × 23 × 25 cm), occupying 80% of the thoracic cavity and causing significant pulmonary compression and mediastinal shift. A multidisciplinary tumor board recommended surgical resection.

RESULTS: Initial uniportal video-assisted thoracic surgery exploration confirmed no pleural invasion. This was followed by a posterolateral thoracotomy for complete tumor excision. The patient recovered without complications. Histopathology confirmed DDLPS with complex histological architecture, including both well-differentiated and dedifferentiated sarcomatous components. The patient is disease-free three years postoperatively.

CONCLUSIONS: Our case report emphasizes the requirement of a multidisciplinary approach to treat massive chest malignancy. Complete surgical resection remains the gold standard to obtain long-term survival.

Keywords: mediastinal liposarcoma; dedifferentiated liposarcoma; surgical resection; thoracic surgery; multidisciplinary approach; long-term survival; case report

Introduction

Soft tissue sarcomas are the rarest form of solid tumor malignancy. They account for only 1% of all tumors in the adult population and include more than 50 subtypes. Liposarcoma is an aggressive subtype that accounts for 20% of all adult soft tissue sarcomas [1]. While it can manifest anywhere in the body, its most frequent occurrences are observed in the retroperitoneum and extremities [2]. Although well-differentiated liposarcoma (WDLPS) can recur, up to 10% of WDLPS cases can transform to dedifferentiated liposarcoma (DDLPS), which is more aggressive with higher local recurrence rates and metastatic potential [1].

Additionally, liposarcomas of the mediastinum account for less than 1% of all cases [3]. Herein, we report the successful surgical treatment of an octogenarian woman presenting with a giant DDLPS in the chest.

Case Presentation

An 83-year-old female presented with increasing dyspnea for two months. Her past medical history included ischemic heart disease treated with two coronary stents. A chest X-ray indicated a giant mass involving two-thirds of the left hemithorax with a contralateral shift of the mediastinum. Chest computed tomography (CT) scan revealed a large mass (21 × 23 × 25 cm) with low density in the

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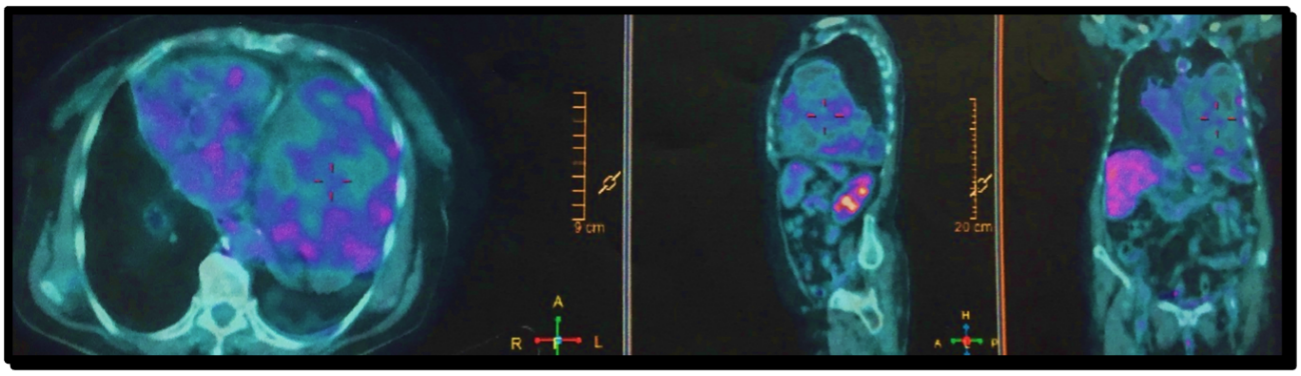

Fig. 1. Positron emission tomography-computed tomography (PET-CT) scan confirmed the huge dimension of the lesion, which appeared to invade the pericardium, the mediastinum, and the hemidiaphragm. A, Anterior; R, Right; L, Left; H, Head; P, Posterior.

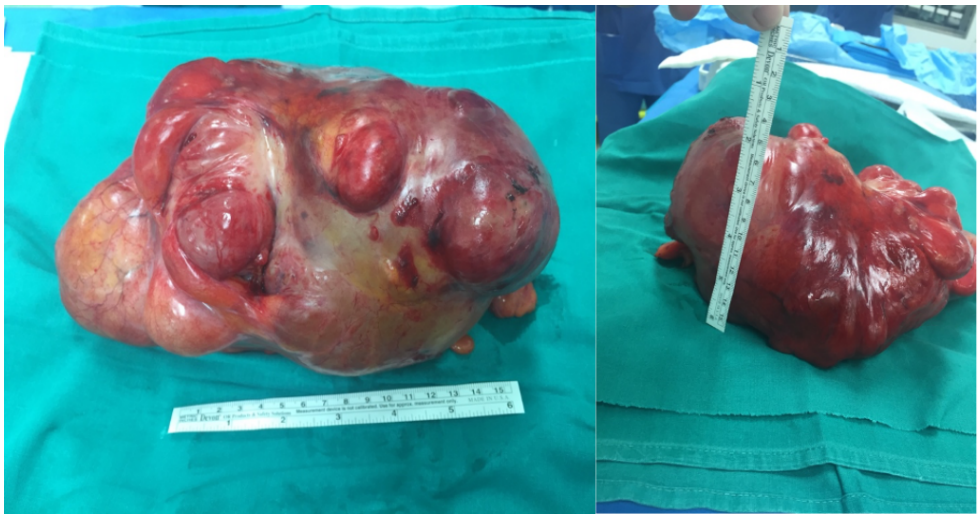

Fig. 2. The massive tumor is extracted from the left chest.

left hemithorax, causing mediastinal shift and pulmonary atelectasis. Positron emission tomography-computed tomography (PET-CT) scan demonstrated moderate uptake by the mass with a Standardized Uptake Value (SUV) of 2.9 (Fig. 1). The preoperative assessment included cardiological evaluation with electrocardiogram and echocardiogram, which revealed an ejection fraction of 65%. Blood and arterial blood gas tests were also conducted, and all were normal. Spirometry was also performed, which showed a forced expiratory volume in 1 second (FEV1) of 1.09 liters and forced vital capacity (FVC) of 1.62 liters, corresponding to 80% and 78% of the predicted values, respectively.

A comprehensive discussion was held during the tumor board meeting, and surgical excision was recommended as the appropriate course of action. The patient was positioned in a full right lateral decubitus position, and anesthesia was maintained using a double-lumen tube. Before thoracotomy, exploratory video-assisted thoracic surgery (VATS) was considered useful for simultaneously assessing and managing the chest involvement by the tumor, and therefore, uniportal VATS was performed. Despite selective ventilation, exploring the chest proved challenging due to the sizable mass. Nevertheless, the absence of pleural involvement or massive mediastinal invasion was noted. A posterolateral thoracotomy was then performed at the sixth intercostal space. The 7th rib was cut posteriorly to obtain more space to remove the mass. The lesion was discovered to occupy about 80% of the thoracic cavity. Additionally, the left lower lobe and part of the upper lobe were noted to be atelectatic. An ultrasonic scalpel was adopted to facilitate the dissection of tight adhesions between the lesion and the pericardium, mediastinum, diaphragm, and left upper lobe of the lung. The mass was found to originate with a large, vascularized pedicle from the anterior mediastinum. The pedicle was sectioned using a vascular endostapler and the mass was removed (Fig. 2). The left lung was subsequently fully re-expanded, and a chest drain was inserted. Blood loss was minimal. The patient experienced no postoperative complications and was discharged on the sixth postoperative day. During the 4-year follow-up, the patient has been healthy with no recurrence. As the patient was an octogenarian and the tumor was macroscopically completely resected, in the absence of guidelines, the multidisciplinary team decided on the “wait and see” method.

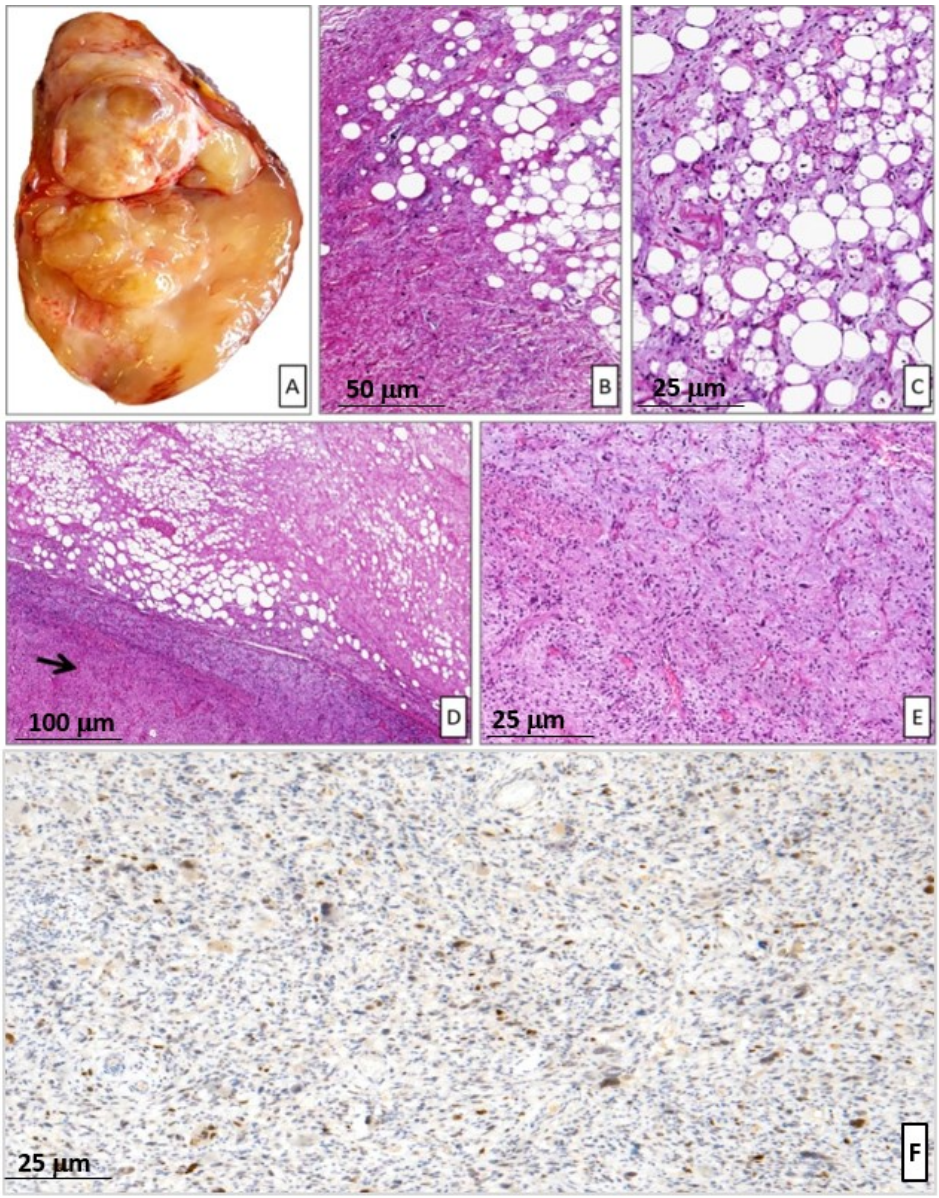

Fig. 3. Microscopic structure of the lesion. (A) The cut surface of the tumor was multinodular, soft in consistency, yellowish in color, and with diffuse myxoid changes. (B) Well-differentiated liposarcoma: variable-sized adipocytes were set in a fibrous stroma containing atypical stromal cells (hematoxylin and eosin; original magnification 100×). (C) Well-differentiated liposarcoma: numerous multivacuolated lipoblasts were set in a prominent myxoid stroma (hematoxylin and eosin; original magnification, 200×). (D) Low magnification showing the abrupt transition from well-differentiated liposarcoma (WDLPS) to non-lipogenic sarcoma, i.e., the dedifferentiated component (arrow) (hematoxylin and eosin; original magnification 50×). (E) The dedifferentiated component was reminiscent of moderate/high-grade myxofibrosarcoma, being composed of atypical spindle to stellate-shaped cells set in a fibro-myxoid stroma rich in thin-walled curvilinear blood vessels (hematoxylin and eosin; original magnification 200×). (F) Diffuse immunohistochemical expression of Mouse double minute 2 homolog (MDM2) is shown (immunoperoxidase; original magnification 200×).

Pathological Findings

Gross examination revealed a large, well-circumscribed, but unencapsulated, fatty tumor mass measuring 25 cm in its greatest diameter. On the cut surface, the tumor showed diffuse myxoid changes along with nodular areas (Fig. 3A). Histological examination on hematoxylin and eosin-stained sections revealed a fatty neoplasm with the typical features of a WDLPS with diffuse myxoid stromal changes. It was composed of both adipocytes, variable in size and shape (Fig. 3B), and numerous multivacuolated and, less frequently, univacuolated lipoblasts (Fig. 3C). In certain areas, both adipocytes and lipoblasts were set in a fibrous stroma containing numerous atypical/bizarre, mono- or multi-nucleated stromal cells (Fig. 3B). In other regions, both lipoblasts and atypical/bizarre stromal cells were embedded within an abundant myxoid stroma (Fig. 3C). Nu-

merous foci of tumor necrosis were also seen (not shown). Although the extensive myxoid stroma could be reminiscent of myxoid liposarcoma, this possibility was ruled out by the presence of fibrous areas with atypical stromal cells, a characteristic feature of WDLPS. In addition, the small spindled, stellate-to-ovoid cells, along with an arborizing/plexiform capillary vasculature, which are morphological clues for the diagnosis of myxoid liposarcoma, were both lacking (Fig. 3B,C). Notably, in some tumor areas, WDLPS showed abrupt or gradual transitions to non-lipogenic sarcoma (Fig. 3D). This tumor component was composed of atypical hyperchromatic, spindle to stellate-shaped cells, focally arranged in short fascicles and set in a variably fibro-myxoid stroma containing numerous thin-walled, arborizing/curvilinear vessels (Fig. 3E). The overall picture of this tumor component was closely reminiscent of an intermediate/high-grade myxofibrosarcoma. Immunohistochemically, neoplastic cells exhibited diffuse expression of vimentin, while α-smooth muscle actin, desmin, cell-surface protein 34 (CD34), Signal Transducer and Activator of Transcription 6 (STAT6), Epithelial membrane antigen (EMA), pancytokeratins, and S100 protein were negative. Immunohistochemical analysis for Mouse double minute 2 homolog (MDM2) protein was also carried out, which showed a diffuse MDM2 expression in the neoplastic cells (Fig. 3F). Based on both the presence of a predominant component (about 70% of the entire tumor mass) of WDLPS containing areas of intermediate/high-grade non-lipogenic sarcoma and the diffuse MDM2 immunohistochemical expression, the final diagnosis of "dedifferentiated liposarcoma" was rendered. Surgical resection margins were focally positive. The case Report adherence to CARE Guidelines (**Supplementary Material**).

Discussion

Soft tissue sarcomas are primary malignant tumors of mesenchymal origin, chiefly originating from all the extra-skeletal soft tissues, including fibrous, adipose, vascular, nervous, synovial, and muscular tissue. Some of the prevalent histologies of soft tissue sarcomas include "sarcoma, not otherwise specified" (20.6%), liposarcoma (16.8%), leiomyosarcoma (13.3%), fibrosarcoma (7.6%), and malignant fibrous histiocytoma (7.4%) [4]. Liposarcomas can be subtyped into four categories based on their clinicopathological and molecular genetic characteristics. These include atypical lipomatous tumors (ALT) or WDLPS, DDLPS, myxoid/round cell liposarcoma, and pleomorphic liposarcoma [5].

The clinical behavior of liposarcoma ranges from an indolent, non-metastasizing disease to aggressive subtypes that can recur and metastasize rapidly. Moreover, it is established that liposarcomas exhibit a gradual growth pattern, and the resulting mass can cause displacement of surrounding structures. In our case, the manifestation of dyspnea was attributed to lung compression. This aligns with a systematic review conducted by Kiełbowski *et al*. [6], which discerned that the predominant manifestations of intrathoracic liposarcoma include dyspnea, chest pain, and cough. Therefore, accurate diagnosis and staging, using a multidisciplinary approach, are crucial for establishing appropriate management and prognosis [7]. Given that the PET-CT ruled out distant metastasis, a preoperative histologic diagnosis was not performed due to significant mediastinal shift (Fig. 1) and worsening symptoms. This was done to avoid delays and expedite the indicated surgical management. The discrepancy between the high-grade dedifferentiation and the low SUV (2.9) of the PET could be justified by the intratumoral necrosis.

The standard treatment recommended in the literature for liposarcoma with no distant metastasis is complete resection [6]. Additionally, we propose conducting an explorative uniportal thoracoscopy to rule out pleural and mediastinal seeding, hence avoiding unnecessary thoracotomy [8,9]. In cases of extensive surrounding structure involvement where complete resection might be challenging, en bloc debulking has been proposed [10]. The role of radiation and chemotherapy as neoadjuvant or adjuvant therapy has also been studied. Livingston *et al*. [11] utilized combination chemotherapy for managing retroperitoneal DDLPS. They discovered a response rate and clinical benefit rate of 24% and 44% respectively, with a 55% mortality and a median overall survival of 29 months [11]. Le Cesne *et al*. [12] conducted a randomized controlled trial on the use of Doxorubicin-based adjuvant chemotherapy, which concluded that the primary prognostic factor for the efficacy of adjuvant chemotherapy is the quality of the initial surgical resection. A multivariate analysis noted that adjuvant chemotherapy, compared to surgery alone and surgery with radiation, resulted in an increased probability of mortality of 11.7% and 89.6%, respectively [5]. This was attributed to a possibly limited responsiveness of DDLPS to chemotherapy or the fact that chemotherapy is generally employed in cases of advanced or metastatic disease. Furthermore, numerous clinical trials support the efficacy of targeted therapy for DDLPS, such as trabectedin, eribulin, and pazopanib for advanced liposarcoma and DDLPS [13].

Our patient is well four years after surgery, exhibiting no signs of recurrence or late complications. Notably, there is insufficient literature regarding the survival data of individuals with thoracic liposarcoma, emphasizing the need for more research in this domain, such as molecular monitoring for potential recurrence. Nevertheless, 6 months of X-rays, yearly CT scan, and if necessary, a PET scan are mandatory in the follow-up to rule out recurrence. Gootee *et al*. [5] demonstrated that liposarcoma of the thorax or trunk has a 5-year survival of 58.9%, with superior outcomes obtained in patients younger than 50 years old and tumors measuring less than 10 cm. Bock *et al*. [2] conducted a population-based study for liposarcoma from 2001 to 2016, reporting a 5-year survival rate of 57.2% for DDLPS. One

of the limitations is the 5-year survival rates for younger age clusters. Spontaneous regression of a DDLPS of the chest wall has also been reported, linked to a high CD8+ infiltrate and a significant positive ratio of Programmed cell-death Ligand 1 (PD-L1). Nevertheless, eventual surgical excision was performed to rule out malignancy [14]. In our case, the malignancy exhibited an absence of distant metastasis. Moreover, the patient experienced compression of surrounding anatomical structures and the tumor was intraoperatively discovered not to invade the mediastinum. Therefore, a macroscopic complete surgical resection was performed. Future research directions and potential breakthroughs for the different pathological subtypes of mediastinal liposarcoma include the writing of expert opinion or even dedicated guidelines discussing the role of radiation, chemotherapy, or targeted therapies.

Conclusions

Liposarcomas are a subset of soft tissue sarcomas that exhibit diverse histological subtypes. While complete resection is the conventional approach outlined in the literature, en bloc debulking may also be performed in cases of extensive surrounding tissue involvement. Additionally, there are ongoing advancements in the roles of radiation therapy, chemotherapy, and targeted therapies. However, the lack of comprehensive literature on the survival data, particularly for DDLPS, necessitates further research.

Availability of Data and Materials

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

Conception and design: MM, MN; review of literature: JAK, MUA, TA and MN; data interpretation: JAK, MUA, TA, MN, GB, GM and MM. Manuscript-original writing and drafting: JAK, MUA, TA, MN, GB, GM and MM. JAK, MUA, MN, and MM contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethical Approval is exempted in the case of a case report as per the IRB center at University of Catania. Written informed consent was obtained from the patient for participation in this case report and for any accompanying images.

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Conflict of Interest

Marcello Migliore is serving as one of the Editorial Board Members of this journal. We declare that Marcello Migliore had no involvement in the peer review of this article and has no access to information regarding its peer review. Other authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62713/aic.4072.

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